

We claim:

1. An oligonucleotide consisting essentially of a nucleotide sequence complementary to a region of RNA or DNA of an infectious agent, wherein the region of RNA or DNA is selected from the group consisting of regions necessary for replication of the infectious agent, regions necessary for gene expression of the infectious agent, and regions necessary for both replication of the infectious agent and gene expression of the infectious agent, wherein anywhere from one to all internal phosphate groups of said oligonucleotide are modified.
2. An oligonucleotide according to claim 1 wherein said oligonucleotide is modified at the internal phosphate group or groups so as to increase uptake of the oligonucleotide into cells, to inhibit degradation of the oligonucleotide within cells, to prevent use of the oligonucleotide as a primer by reverse transcriptase, to increase the strength of binding of the oligonucleotide to a region of RNA or DNA of the infectious agent, or any combination thereof.
3. An oligonucleotide of claim 2, wherein said oligonucleotide is modified at the internal phosphate group or groups so as to inhibit degradation of said oligonucleotide inside cells.
4. An oligonucleotide of claim 1 having from 8 to 50 nucleotides.
5. An oligonucleotide of claim 1 having from 14 to 26 nucleotides.
6. An oligonucleotide of claim 1, wherein only the two 3'-most and two 5'-most internal phosphate groups are modified.
7. An oligonucleotide of claim 1, wherein all the internal phosphate groups are modified.

8. An oligonucleotide of claim 1, wherein all the internal phosphate groups are modified so as to inhibit degradation of said oligonucleotide inside cells.
9. An oligonucleotide consisting essentially of a nucleotide sequence complementary to a region of RNA or DNA of a virus, wherein the region of RNA or DNA is selected from the group consisting of regions necessary for replication of the virus, regions necessary for gene expression of the virus, and regions necessary for both replication of the virus and gene expression of the virus, wherein anywhere from one to all internal phosphate groups of said oligonucleotide are modified.
10. An oligonucleotide according to claim 9 wherein said oligonucleotide is modified at the internal phosphate group or groups so as to increase uptake of the oligonucleotide into cells, to inhibit degradation of the oligonucleotide within cells, to prevent use of the oligonucleotide as a primer by reverse transcriptase, to increase the strength of binding of the oligonucleotide to a region of RNA or DNA of the virus or any combination thereof.
11. An oligonucleotide of claim 10, wherein said oligonucleotide is modified at the internal phosphate group or groups so as to inhibit degradation of said oligonucleotide inside cells.
12. An oligonucleotide of claim 9 having from 8 to 50 nucleotides.
13. An oligonucleotide of claim 9 having from 14 to 26 nucleotides.
14. An oligonucleotide of claim 9, wherein only the two 3'-most and two 5'-most internal phosphate groups are modified.

15. An oligonucleotide of claim 9, wherein all the internal phosphate groups are modified.

16. An oligonucleotide of claim 9, wherein all the internal phosphate groups are modified so as to inhibit degradation of said oligonucleotide inside cells.

sub
17. An oligonucleotide consisting essentially of a nucleotide sequence complementary to a region of RNA or DNA of HTLV-III, wherein the region of RNA or DNA is selected from the group consisting of regions necessary for replication of HTLV-III, regions necessary for gene expression of HTLV-III, and regions necessary for both replication of HTLV-III and gene expression of HTLV-III, wherein anywhere from one to all internal phosphate groups of said oligonucleotide are modified.

18. An oligonucleotide according to claim 17 wherein said oligonucleotide is modified at the internal phosphate group or groups so as to increase uptake of the oligonucleotide into cells, to inhibit degradation of the oligonucleotide within cells, to prevent use of the oligonucleotide as a primer by reverse transcriptase, to increase the strength of binding of the oligonucleotide to a region of RNA or DNA of HTLV-III or any combination thereof.

19. An oligonucleotide of claim 18, wherein said oligonucleotide is modified at the internal phosphate group or groups so as to inhibit degradation of said oligonucleotide inside cells.

~~20. An oligonucleotide of claim 17 having from 8 to 50 nucleotides.~~

21. An oligonucleotide of claim 17 having from 14 to 26 nucleotides.

22. An oligonucleotide of claim 17, wherein only the two 3'-most and two 5'-most internal phosphate groups are modified.

23. An oligonucleotide of claim 17, wherein all the internal phosphate groups are modified.

24. An oligonucleotide of claim 17, wherein all the internal phosphate groups are modified so as to inhibit degradation of said oligonucleotide inside cells.

25. An oligonucleotide of Claim 17, wherein the nucleotide sequence is complementary to a region of the HTLV-III genome selected from the group consisting of:

- a) the tRNA^{lys} primer binding site;
- b) regions of the HTLV-III genome vicinal in the 5' direction to the tRNA^{lys} primer binding site;
- c) the mRNA donor splice sites;
- d) the mRNA acceptor splice sites;
- e) the initiator codon for the *gag* gene;
- f) the initiator codon for the *env* gene;
- g) the initiator codon for the *tat* gene;
- h) the initiator codon for the *sor* gene;
- i) the initiator codon for the 3' orf gene;
- j) the cap nucleotide of the HTLV-III genome;
- k) the *art* gene or portions thereof; and
- l) the region of the HTLV-III genome encoding a frameshift.

~~26. An oligonucleotide of claim 25 having from 8 to 50 nucleotides.~~

27. An oligonucleotide of claim 25 having from 14 to 26 nucleotides.

~~28. An oligonucleotide according to claim 1, wherein the modified internal phosphate group is a phosphorothioate group.~~

~~29. An oligonucleotide according to claim 2, wherein the modified internal phosphate group is a phosphorothioate group.~~

~~30. An oligonucleotide according to claim 3, wherein the modified internal phosphate group is a phosphorothioate group.~~

~~31. An oligonucleotide according to claim 4, wherein the modified internal phosphate group is a phosphorothioate group.~~

~~32. An oligonucleotide according to claim 5, wherein the modified internal phosphate group is a phosphorothioate group.~~

~~33. An oligonucleotide according to claim 6, wherein the modified internal phosphate group is a phosphorothioate group.~~

~~34. An oligonucleotide according to claim 7, wherein the modified internal phosphate group is a phosphorothioate group.~~

~~35. An oligonucleotide according to claim 8, wherein the modified internal phosphate group is a phosphorothioate group.~~

36. An oligonucleotide according to claim 9, wherein the modified internal phosphate group is a phosphorothioate group.

37. An oligonucleotide according to claim 10, wherein the modified internal phosphate group is a phosphorothioate group.

38. An oligonucleotide according to claim 11, wherein the modified internal phosphate group is a phosphorothioate group.

39. An oligonucleotide according to claim 12, wherein the modified internal phosphate group is a phosphorothioate group.

40. An oligonucleotide according to claim 13, wherein the modified internal phosphate group is a phosphorothioate group.

41. An oligonucleotide according to claim 14, wherein the modified internal phosphate group is a phosphorothioate group.

42. An oligonucleotide according to claim 15, wherein the modified internal phosphate group is a phosphorothioate group.

43. An oligonucleotide according to claim 16, wherein the modified internal phosphate group is a phosphorothioate group.

44. An oligonucleotide according to claim 17, wherein the modified internal phosphate group is a phosphorothioate group.

sub
a3

Sub 3
Q3
45. An oligonucleotide according to claim 18, wherein the modified internal phosphate group is a phosphorothioate group.

46. An oligonucleotide according to claim 19, wherein the modified internal phosphate group is a phosphorothioate group.

47. An oligonucleotide according to claim 20, wherein the modified internal phosphate group is a phosphorothioate group.

Sub 4
Q4
48. An oligonucleotide according to claim 21, wherein the modified internal phosphate group is a phosphorothioate group.

49. An oligonucleotide according to claim 22, wherein the modified internal phosphate group is a phosphorothioate group.

50. An oligonucleotide according to claim 23, wherein the modified internal phosphate group is a phosphorothioate group.

51. An oligonucleotide according to claim 24, wherein the modified internal phosphate group is a phosphorothioate group.

52. An oligonucleotide according to claim 25, wherein the modified internal phosphate group is a phosphorothioate group.

53. An oligonucleotide according to claim 26, wherein the modified internal phosphate group is a phosphorothioate group.

Sub
25
54. ~~An oligonucleotide according to claim 27, wherein the modified internal phosphate group is a phosphorothioate group.~~

55. An oligonucleotide according to claim 17 selected from the group consisting of the oligonucleotide phosphorothioates represented in Table 3.

56. An oligonucleotide according to claim 44 that is complementary to a region including the initiator codon of the HTLV-III *gag* gene.

~~57. An oligonucleotide of claim 56 having from 8 to 50 nucleotides.~~

58. An oligonucleotide of claim 56 having from 14 to 26 nucleotides.

~~59. A composition for inhibiting the replication of an infectious agent or gene expression of an infectious agent in a cell, said composition comprising an oligonucleotide according to any one of claims 1-8 and a pharmaceutically suitable carrier.~~

60. A composition for inhibiting the replication of a virus or gene expression of a virus in a cell, said composition comprising an oligonucleotide according to any one of claims 9-16 and a pharmaceutically suitable carrier.

Sub
26
~~61. A composition for inhibiting the replication of HTLV-III or gene expression of HTLV-III in a cell, said composition comprising an oligonucleotide according to any one of claims 17-27 and a pharmaceutically suitable carrier.~~

62. A composition for inhibiting the replication of an infectious agent or gene expression of an infectious agent in a cell, said composition comprising an oligonucleotide according to any one of claims 28-35 and a pharmaceutically suitable carrier.

63. A composition for inhibiting the replication of a virus or gene expression of a virus in a cell, said composition comprising an oligonucleotide according to any one of claims 36-43 and a pharmaceutically suitable carrier.

64. A composition for inhibiting the replication of HTLV-III or gene expression of HTLV-III in a cell, said composition comprising an oligonucleotide according to any one of claims 44-58 and a therapeutically suitable carrier.

65. A method of inhibiting the replication of an infectious agent or gene expression of an infectious agent or both in a cell, said method comprising contacting the cell with an effective amount of an oligonucleotide according to any one of claims 1-8.

66. A method of inhibiting the replication of a virus or gene expression or both of a virus in a cell infected with the virus, said method comprising contacting the cell with an effective amount of an oligonucleotide according to any one of claims 9-16.

67. A method of inhibiting the replication of HTLV-III or gene expression of HTLV-III or both in a cell infected with HTLV-III, said method comprising contacting the cell with an effective amount of an oligonucleotide according to any one of claims 17-27.

68. A method of inhibiting the replication of an infectious agent or gene expression of an infectious agent or both in a cell, said method comprising contacting the cell with an effective amount of an oligonucleotide according to any one of claims 28-35.

69. A method of inhibiting the replication of a virus or gene expression of a virus or both in a cell infected with the virus, said method comprising contacting the cell with an effective amount of an oligonucleotide according to any one of claims 36-43.

70. A method of inhibiting the replication of HTLV-III or gene expression of HTLV-III or both in a cell infected with HTLV-III, said method comprising contacting the cell with an effective amount of an oligonucleotide according to any one of claims 44-58.